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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,577	06/26/2003	Molly Accola	FORS-08167	4684

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Mary Ann Brow
MEDLEN & CARROLL, LLP
Suite 350
101 Howard Street
San Francisco, CA 94105

EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 08/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/606,577	ACCOLA ET AL.	
	Examiner	Art Unit	
	Jeanine A. Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-4 and 15-19* is/are pending in the application.

4a) Of the above claim(s) *15-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed June 27, 2005 Currently, claims 1-4, 15-19 are pending. Claims 15-19 have been withdrawn as drawn to non-elected subject matter.

Election/Restrictions

2. Applicant's election with traverse of a mutation 2184delA, Claims 1-4 in the paper filed June 27, 2005 is acknowledged.

The response asserts that MPEP 803.04 relates to nucleic acid sequences and requires the Patent office to search a reasonable number of sequences. Here, the claims are not specifically drawn to sequences. Further, a search for a mutation with in a gene requires not only a sequence search but also an extensive search of the literature including tables found in the literature.

The requirement is still deemed proper and is therefore made FINAL.

This application contains claims 15-19 are drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

3. This application claims priority to US application 10/371,913, filed February 21, 2003 and provisional application 60/426,114, filed November 14, 2002.

Drawings

4. The drawings are acceptable.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-4 are drawn to a kit comprising a non-amplified oligonucleotide detection assay configured for detecting CFTR alleles selected from the group consisting of 2184delA or the wild-type version thereof is unclear. It is unclear how a kit can comprise an assay. A kit is a product. A kit would seem to contain elements, however the claim does not set forth any elements contained within the kit. An assay would appear to be most closely related to a method. It is unclear how a kit may

comprise an assay/method. It would seem like a kit could comprise the elements needed for an assay.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Boehringer Mannheim (1997 Biochemicals Catalog, page 95).

Boehringer Mannheim teaches non-radioactive labeling and detection of nucleic acids. Boehringer Mannheim sells kits comprising hybridization bags, nylon membranes, and digoxienin-3-O-methyicarbonyl, for example.

Boehringer Mannheim teaches that the hybridization bags can be used in non-radioactive hybridization and detection procedures, standard radioactive probe hybridization and Western blotting procedures. Thus, these hybridization bags would constitute a kit comprising a non-amplified oligonucleotide detection assay configured for detecting CFTR alleles.

Boehringer Mannheim teaches nylon membranes are ideal for Southern, Northern, and dot blots for DNA, RNA or oligonucleotide probes. Thus, these nylon

membranes would constitute a kit comprising an assay with the intended purpose of detecting CFTR allele 2184delA.

Boehringer Mannheim finally teaches digoxienin-3-O-methyicarbonyl which is suitable for 5' end labeling of oligonucleotides. A label would be configured to detect a CFTR allele 2184delA, for example.

Thus, Boehringer Mannheim teaches a number of kit products comprising a non-amplified oligonucleotide detection assay for detecting alleles.

7. Claims rejected under 35 U.S.C. 102(b) as being anticipated by Sigma-Aldrich Techware Laboratory Equipment and Supplies (1995-1996, page 213).

Sigma-Aldrich teaches a nucleic acid sequencing unit which allows sequencing of nucleic acids. Sigma-Aldrich teaches the sequencing unit may be fixed-height, adjustable-height or dual gel. The sequencing unit of Sigma-Aldrich would constitute a kit comprising an assay for detecting CFTR allele 2184delA.

8. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Shuber (US 5,834,181, November 10, 1998).

Shuber teaches high throughput screening methods for sequences or genetic alterations in nucleic acids. Shuber teaches a kit for carrying out high-throughput screening of nucleic acid samples. The kit includes, in packaged combination, at least the following components: a support, a multiplicity of purine and pyrimidine containing polymers, appropriate labeling components, and enzymes and reagents required for

polymer sequence determination (col. 11, lines 55-62). Shuber teaches hybridization with allele-specific oligonucleotides (ASOs) for specific mutations. The allele specific oligonucleotides (ASOs) were 17mers synthesized and HPLC-purified. Shuber teaches examples of ASOs representing known cystic fibrosis mutations (co. 18, lines 42-45). Shuber specifically teaches ASO probes for 2184delA (col. 19, lines 15). Thus, Shuber teaches a kit comprising a non-amplified detection assay configured for detecting CFTR allele 2184delA or the wild-type version thereof.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 2-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuber (US 5,834,181, November 10, 1998) and Fors et al. (Pharmacogenomics, Vol. 1, No. 2, pages 219-229, 2000).

Shuber teaches high throughput screening methods for sequences or genetic alterations in nucleic acids. Shuber teaches a kit for carrying out high-throughput screening of nucleic acid samples. The kit includes, in packaged combination, at least the following components: a support, a multiplicity of purine and pyrimidine containing polymers, appropriate labeling components, and enzymes and reagents required for polymer sequence determination (col. 11, lines 55-62). Shuber teaches hybridization with allele-specific oligonucleotides (ASOs) for specific mutations. The allele specific oligonucleotides (ASOs) were 17mers synthesized and HPLC-purified. Shuber teaches examples of ASOs representing known cystic fibrosis mutations (co. 18, lines 42-45). Shuber specifically teaches ASO probes for 2184delA (col. 19, lines 15). Thus, Shuber teaches a kit comprising a non-amplified detection assay configured for detecting CFTR allele 2184delA or the wild-type version thereof.

Fors teaches large-scale SNP scoring from unamplified genomic DNA. Fors teaches the Invader assay offers a simple diagnostic platform to detect single nucleotide changes with high specificity and sensitivity from unamplified, genomic DNA. The Invader assay uses a structure-specific 5' nuclease (or flap endonuclease) to cleave sequence-specific structures in each of two cascading reactions. The cleavage structure forms when two synthetic oligonucleotide probes hybridize in tandem to a target. Fors teaches that the signal amplification permits identification of single base

changes directly from genomic DNA without prior amplification (abstract). The Invader technology is in routine use today for high-throughput SNP screening. The technology involves a simple, cascading reaction that can detect mutations and SNPs directly from unamplified genomic DNA or RNA in a homogeneous, isothermal, FRET-based format (page 222). Figure 1 illustrates the schematic of the Invader assay which contains various oligonucleotides including an oligonucleotide which comprises various 5' and 3' poritions that do not hybridize to target sequences. The technology is readily adapted to different sequences since the unlabeled analyte-specific oligonucleotides used in the primary reaction; no new dye-labelled oligonucleotides are needed (page 223, col. 1). This creates a streamlined approach to creating new assays allows rapid and accurate synthesis, purification and quantification of new SNP assay sets.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the ASO solid support method of Shuber with the Invader method of Fors for detecting the 2184delA mutation in the cystic fibrosis gene. The ordinary artisan would have been motivated to have detected the well known 2184delA mutation in the cystic fibrosis gene using the Invader assay. Fors specifically teaches the Invader method is a simple diagnostic platform to detect single nucleotide changes with high specificity and sensitivity from unamplified, genomic DNA. For the expected benefits taught by Fors, the ordinary artisan would have been motivated to have modified the method of Shuber to obtain the claimed invention as a whole.

Alternatively, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the Invader method taught by Fors for the mutation detection of 2184delA taught by Shuber. Fors specifically teaches that the Invader technology is readily adapted to different sequences since the unlabeled analyte-specific oligonucleotides used in the primary reaction; no new dye-labelled oligonucleotides are needed (page 223, col. 1). This creates a streamlined approach to creating new assays allows rapid and accurate synthesis, purification and quantification of new SNP assay sets. The ordinary artisan would have been motivated to have detected alternative SNPs or mutations including the 2184delA mutation taught by Shuber as involved in cystic fibrosis for the benefit of quickly detecting a known mutation.

11. Claims 2-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuber (US 5,834,181, November 10, 1998) and Fors et al. (US 2003-0152942A1, August 2003).

Shuber teaches high throughput screening methods for sequences or genetic alterations in nucleic acids. Shuber teaches a kit for carrying out high-throughput screening of nucleic acid samples. The kit includes, in packaged combination, at least the following components: a support, a multiplicity of purine and pyrimidine containing polymers, appropriate labeling components, and enzymes and reagents required for polymer sequence determination (col. 11, lines 55-62). Shuber teaches hybridization with allele-specific oligonucleotides (ASOs) for specific mutations. The allele specific

oligonucleotides (ASOs) were 17mers synthesized and HPLC-purified. Shuber teaches examples of ASOs representing known cystic fibrosis mutations (co. 18, lines 42-45). Shuber specifically teaches ASO probes for 2184delA (col. 19, lines 15). Thus, Shuber teaches a kit comprising a non-amplified detection assay configured for detecting CFTR allele 2184delA or the wild-type version thereof.

Fors teaches nucleic acid detection in pooled samples using the INVADER detection assay. Figure 1 illustrate the schematics of Invader Assay. Fors teaches polymorphisms in a sample may be detected using INVADER assay. Figure 3 shows a graph demonstrating the ability of the INVADER assay to detect mutations in the CFTR gene in pooled samples. Fors specifically describes the structure of the INVADER assay probes (para 54-55). Fors further teaches the INVADER assay reagents are provided in a kit for the storage, transport or delivery of reaction reagents and supporting materials to a location (para 60). Example 2 is specifically directed to CFTR detection by the INVADER assay in pooled samples. The CFTR gene is analyzed for the F508 mutation in the CFTR gene in a pooled sample (para 110-116). Fors teaches the double benefit of reducing the number of assays required to verify a new SNP and of allowing the use of one large, preparation of the pooled DNA to be used for numerous tests, thereby reducing the influence of sample-to sample variations in DNA purity (para 115).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the ASO solid support method of Shuber with the pooled Invader method of Fors for detecting the 2184delA mutation

in the cystic fibrosis gene. The ordinary artisan would have been motivated to have detected the well known 2184delA mutation in the cystic fibrosis gene using the Invader assay. Fors specifically teaches the double benefit of reducing the number of assays required to verify a new SNP and of allowing the use of one large, preparation of the pooled DNA to be used for numerous tests, thereby reducing the influence of sample-to sample variations in DNA purity (para 115). Thus, the ordinary artisan would have been motivated to have used the pooled CFTR mutation analysis for the 21894delA mutation.

Alternatively, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the pooled Invader method taught by Fors for the mutation detection of 2184delA taught by Shuber. Fors specifically teaches that the Invader technology for the F508 mutation within the cystic fibrosis gene. The ordinary artisan would have been motivated to have detected alternative SNPs or mutations including the 2184delA mutation taught by Shuber as involved in cystic fibrosis for the benefit of quickly detecting a known mutation.

Conclusion

12. No claims allowable over the art.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272- 0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

Jeanine Goldberg
Primary Examiner
August 2, 2005